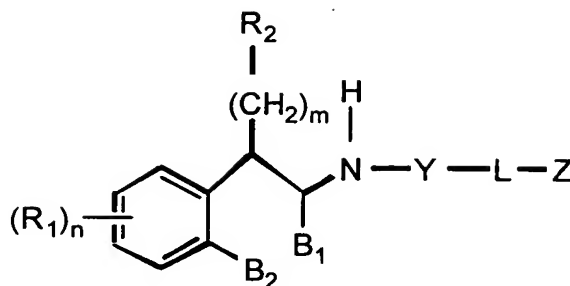


What is claimed is:

A compound of the formula:



A

in which:

a

R_1 is independently selected from the group consisting of hydrogen; hydroxy; halo; C_{1-8} alkyl; substituted C_{1-8} alkyl; C_{1-8} alkoxy; substituted C_{1-8} alkoxy; trifluoroalkyl; C_{1-8} alkylthio; substituted C_{1-8} alkylthio; C_{3-6} cycloalkyl; C_{3-6} cycloalkoxy; nitro; amino; C_{1-6} alkylamino; C_{1-8} dialkylamino; C_{4-8} cycloalkylamino; cyano; carboxy; C_{1-5} alkoxycarbonyl; C_{1-5} alkylcarbonyloxy; formyl; carbamoyl; phenyl; and substituted phenyl;

n is 1-2;

B_1 is hydrogen;

B_2 is hydrogen; or B_1 and B_2 are methylene and joined together to form a five or six membered ring;

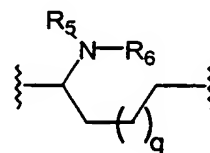
m is 0-3;

R_2 is independently selected from the group consisting of hydrogen; hydroxy; C_{1-6} alkyl; C_{2-6} alkenyl; halo; C_{3-7} cycloalkyl; phenyl; substituted phenyl; naphthyl, substituted naphthyl; phenoxy; substituted phenoxy; heteroaryl; substituted heteroaryl; and heterocycloalkyl;

5

L is selected from the group consisting of C_{1-8} alkylene; C_{2-10} alkenylene; C_{2-10} alkynylene; C_{3-7} cycloalkylene; C_{3-7} cycloalkyl C_{1-4} alkylene; aryl C_{1-4} alkylene; α -amino C_{4-7} alkylene;

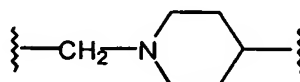
10



(N-methylene)piperidin-4-yl;

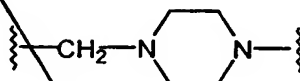
a

15

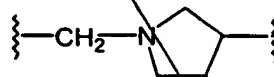


(N-methylene)piperazin-4-yl;

20

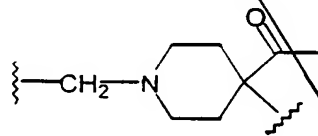


(N-methylene)pyrrolidin-3-yl;

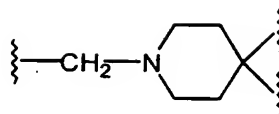


(N-methylene)-4-acetyl-piperidin-4-yl;

25



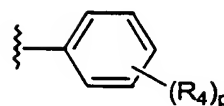
and (N-methylene)piperidin-4,4-diyl;



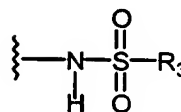
5 Y is methylene or carbonyl;

Z is selected from the group consisting of:

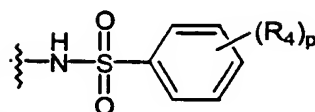
aryl;



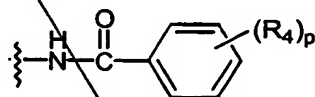
N-sulfonamido;



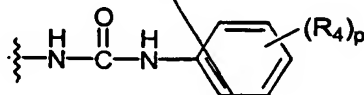
N-(aryl)sulfonamido;



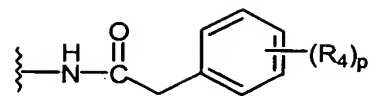
arylamido;



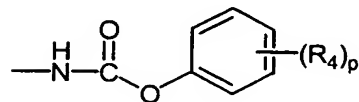
arylureido;



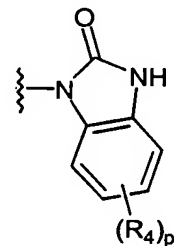
arylacetamido:



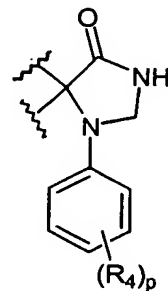
(aryloxy)carbonylamino;



2,3-dihydro-2-oxo-1H-benzimidazol-1-yl;



and 1-aryl-2,3-dihydro-4-oxo-imidazol-5,5-diyl;



a

R_3 is independently selected from the group consisting of C_{1-6} alkyl; substituted C_{1-8} alkyl; cycloalkyl; substituted cycloalkyl; naphthyl; substituted naphthyl; heteroaryl; and substituted heteroaryl;

R_4 is independently selected from the group consisting of hydrogen; C_{1-8} alkyl; C_{1-8} alkoxy; substituted C_{1-8} alkoxy; hydroxy; halogen; cyano; nitro; amino; C_{1-8} alkylamino; and C_{1-8} dialkylamino;

R_5 is independently selected from the group consisting of hydrogen; C_{1-8} alkyl; C_{1-8} alkylcarbonyl; aroyl; carbamoyl; amidino; C_{1-8} alkyl; C_{1-8} alkylaminocarbonyl; (arylamino)carbonyl; and aryl C_{1-8} alkylcarbonyl;

5 R_6 is independently selected from hydrogen and C_{1-8} alkyl;

p is 1-3;

q is 1-3;

10

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

provided that when L is C_{1-6} alkylene; C_{2-10} alkenylene; C_{2-10} alkynylene; C_{3-7} cycloalkylene; C_{3-7} cycloalkyl C_{1-4} alkylene; aryl C_{1-4} alkylene; or α -amino C_{4-7} alkylene; then Z is phenyl, N-sulfonamido or N-(aryl)sulfonamido;

15

when L is (N-methylene)piperazin-4-yl; then Z is phenyl or naphthyl;

20

when L is (N-methylene)pyrrolidin-3-yl or (N-methylene)piperidin-4-yl; then Z is N-sulfonamido; N-(aryl)sulfonamido; 2,3-dihydro-2-oxo-1H-benzimidazol-1-yl; benzamido; phenylureido; phenylacetamido or (phenoxy)carbonylamino;

25

when L is (N-methylene)-4-acetyl-piperidin-4-yl; then Z is phenyl or naphthyl and Y is carbonyl;

when L is (N-methylene)piperidin-4,4-diyl; then Z is 1-aryl-2,3-dihydro-4-oxoimidazol-5,5-diyl and Y is carbonyl;

30

and when B_1 and B_2 are both methylene thus forming a six membered ring and when L is C_{1-10} alkylene; C_{2-10} alkenylene; C_{2-10} alkynylene; or aryl C_{1-4} alkylene; then Z is other than N-sulfonamido, N-(aryl)sulfonamido or phenyl.

2. A compound of claim 1 wherein R₁ is H; alkyl; substituted alkyl; alkoxy; halo; substituted alkoxy; hydroxy; trifluoralkyl; nitro; amino; alkylamino; cycloalkylamino; cyano; carboxy; cycloalkyl; phenyl; and substituted phenyl;

R₂ is H; hydroxy; alkyl; substituted alkyl; halo; heterocycloalkyl; heteroaryl; phenyl; substituted phenyl; naphthyl and substituted naphthyl;

B₁ is hydrogen;

B₂ is hydrogen; or B₁ and B₂ are methylene and joined together to form a five or six membered ring;

Y is methylene or carbonyl;

Z is selected from the group consisting of aryl; substituted aryl; N-sulfonamido; N-(aryl)sulfonamido; substituted N-(aryl)sulfonamido; arylamido; substituted arylamido; arylureido; substituted arylureido; arylacetamido; substituted arylacetamido; (aryloxy)carbonylamino; substituted (aryloxy)carbonylamino; 2,3-dihydro-2-oxo-1H-benzimidazol-1-yl; substituted 2,3-dihydro-2-oxo-1H-benzimidazol-1-yl; 1-aryl-2,3-dihydro-4-oxo-imidazol-5,5-diyl; and substituted 1-aryl-2,3-dihydro-4-oxo-imidazol-5,5-diyl;

L is C₁₋₆alkylene; C₂₋₁₀ alkenylene; C₂₋₁₀ alkynylene; C₃₋₇cycloalkylene;

C₃₋₇cycloalkylC₁₋₄alkylene; arylC₁₋₄ alkylene; α -aminoC₄₋₇alkylene; (N-methylene)piperidin-4-yl; substituted (N-methylene)piperidin-4-yl; (N-methylene)piperazin-4-yl; (N-methylene)pyrrolidin-3-yl; (N-methylene)-4-acetyl-piperidin-4-yl; and (N-methylene)piperidin-4,4-diyl;

n is 1-2;

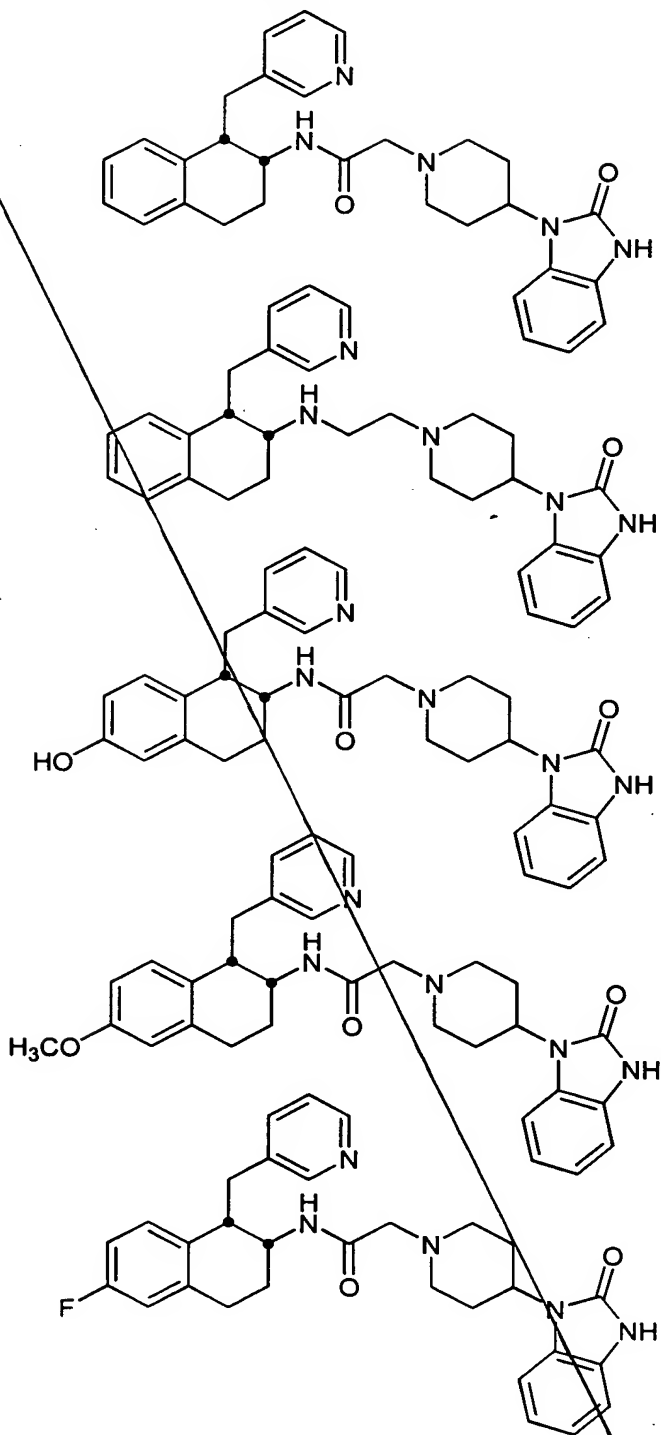
m is 1-3;

contd.
a¹

p is 1-3; and

q is 1-3.

5 3. A compound of claim 1 selected from the group consisting of:

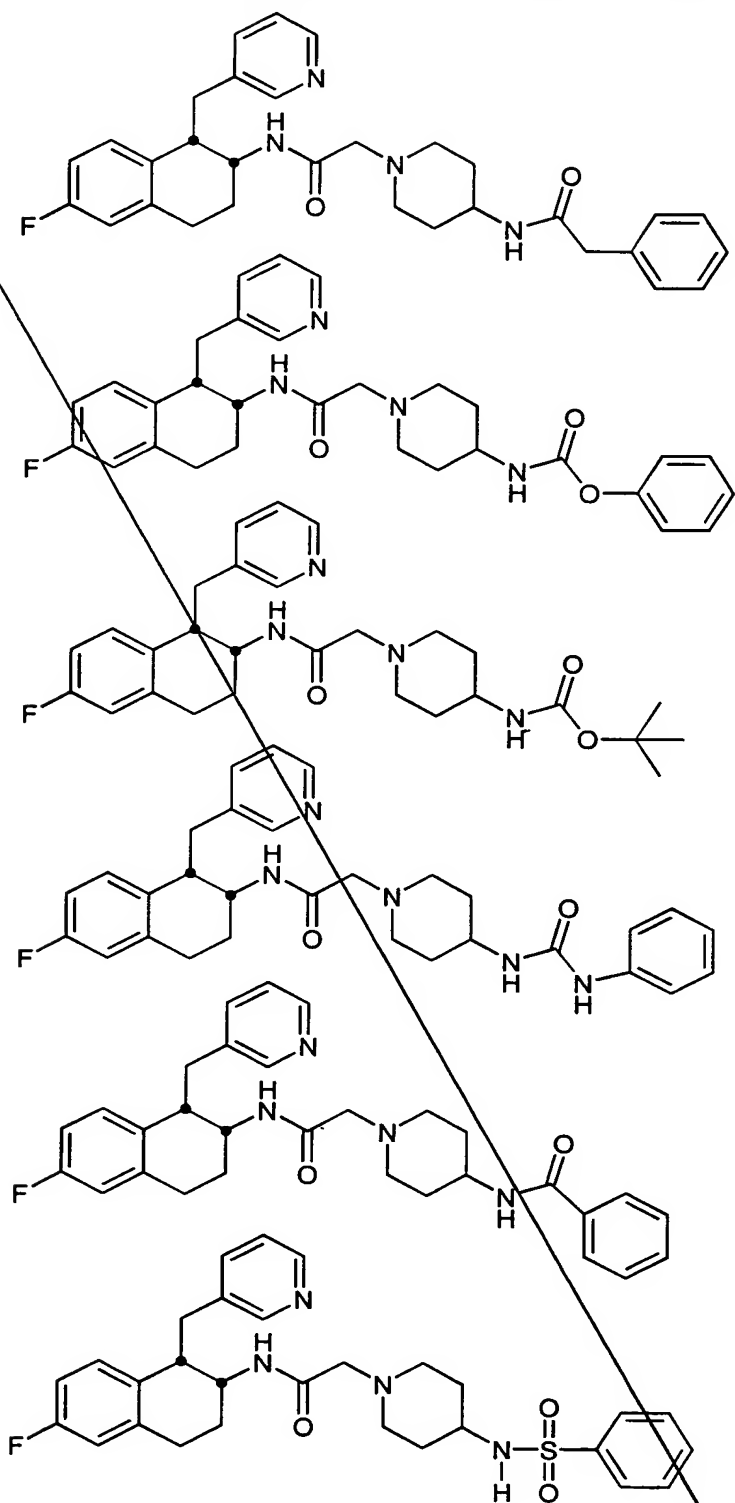


and

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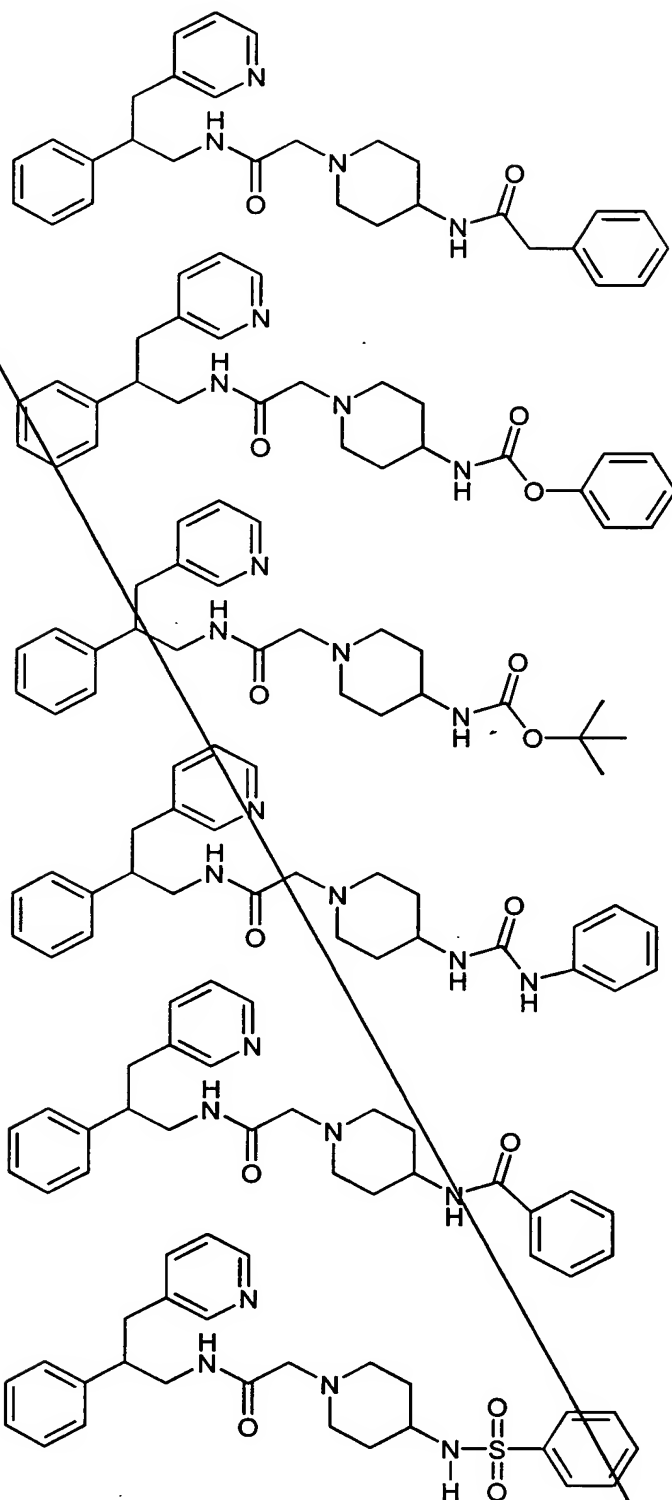
4. A compound of claim 1 selected from the group consisting of:



and

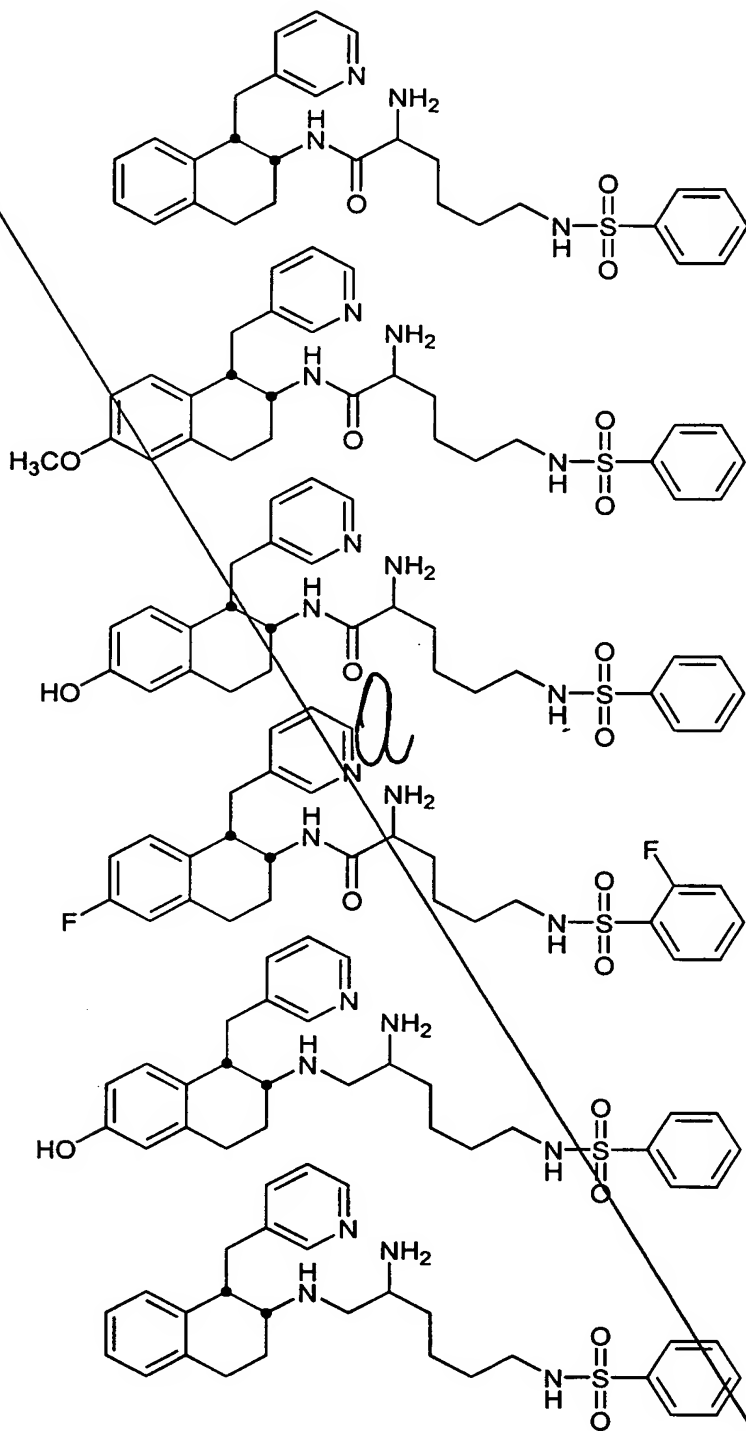
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5. A compound of claim 1 selected from the group consisting of:



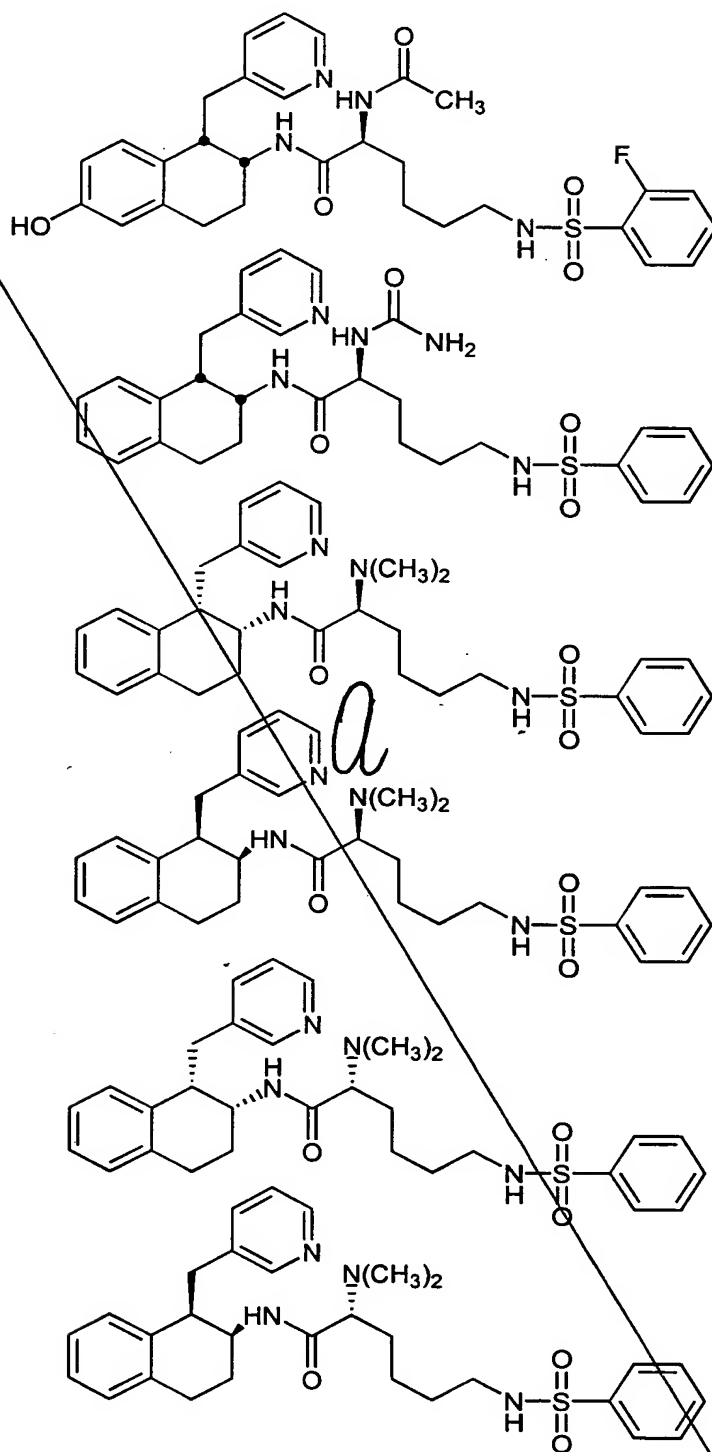
and

6. A compound of claim 1 selected from the group consisting of:



and

A compound of claim 1 selected from the group consisting of:



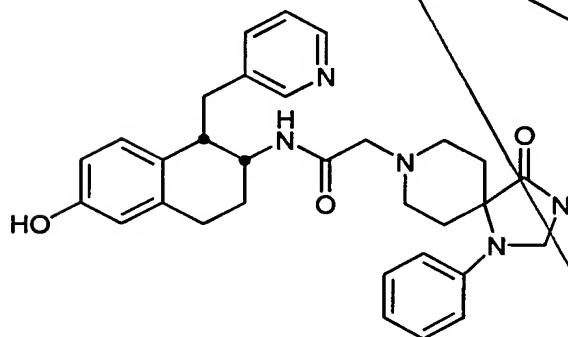
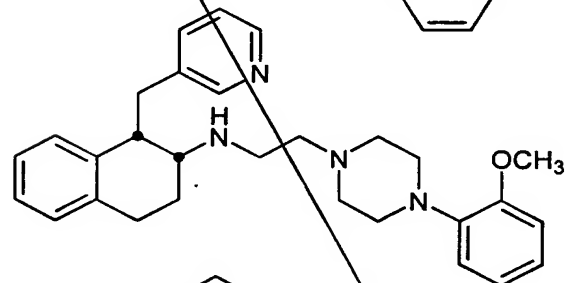
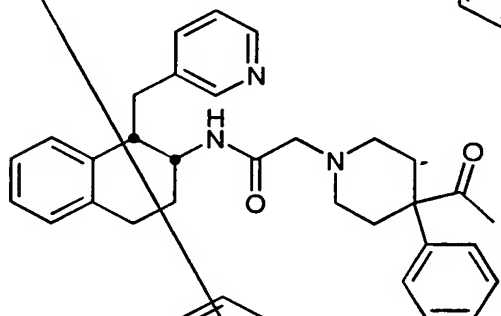
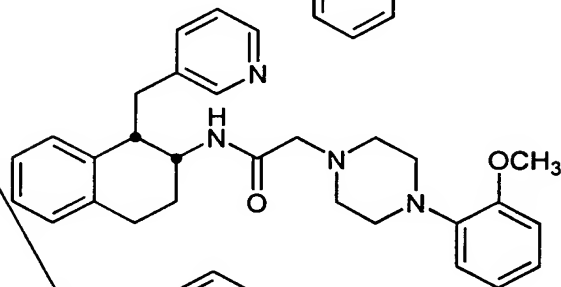
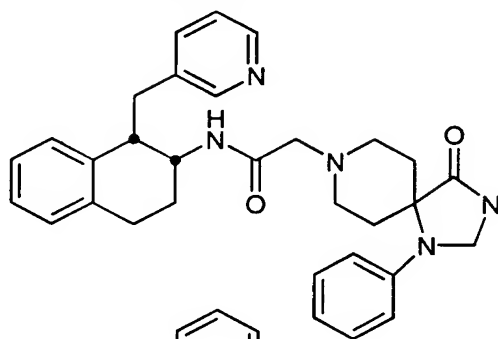
and

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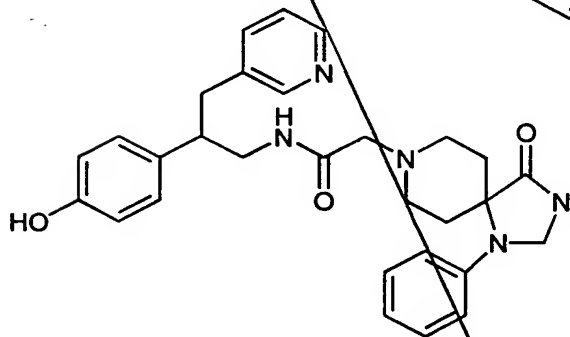
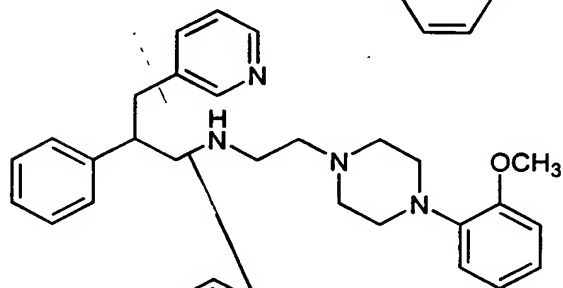
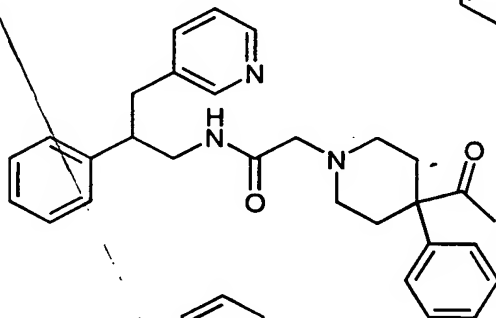
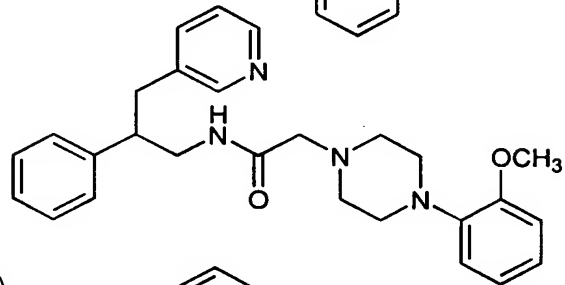
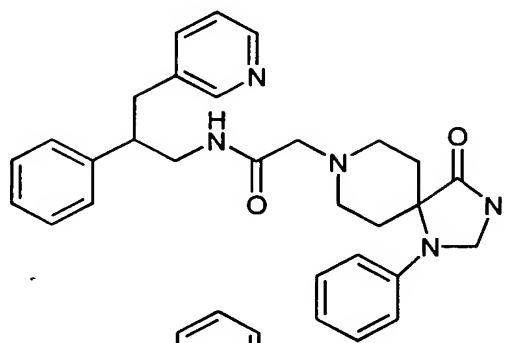
A compound of claim 1 selected from the group consisting of:



and

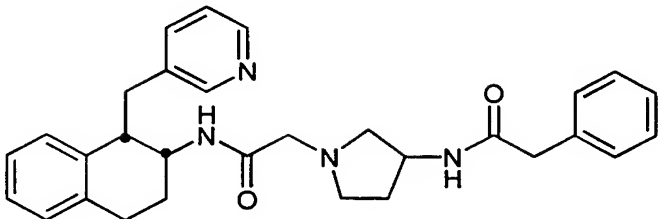
contd.
Q2

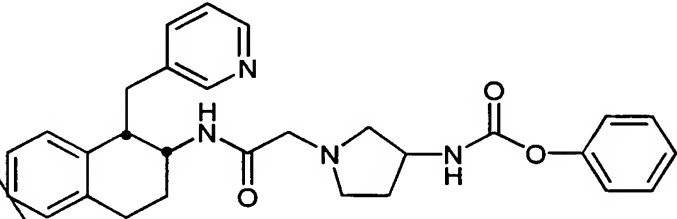
9. A compound of claim 1 selected from the group consisting of:

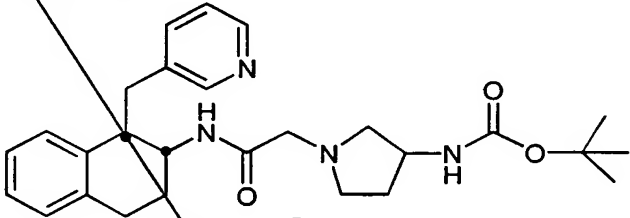


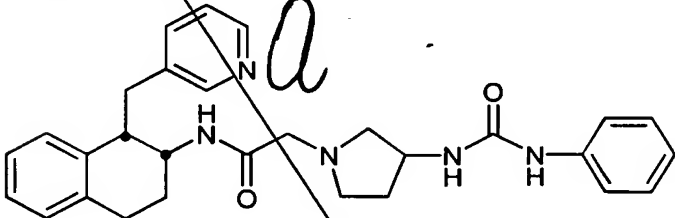
and

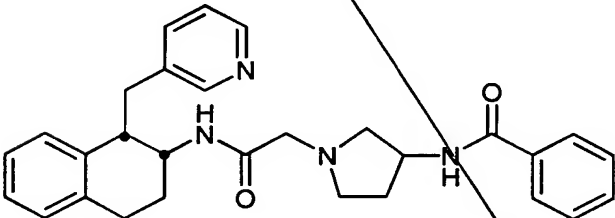
10. A compound of claim 1 selected from the group consisting of:

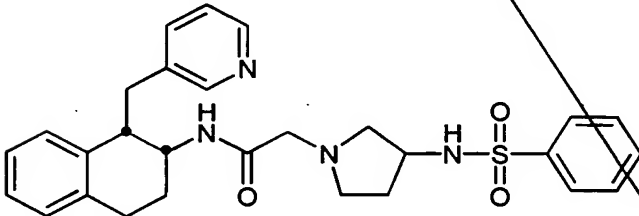
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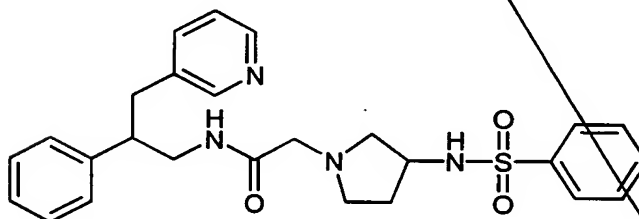
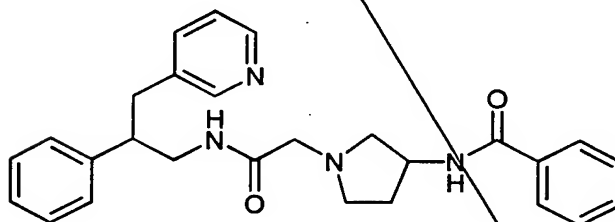
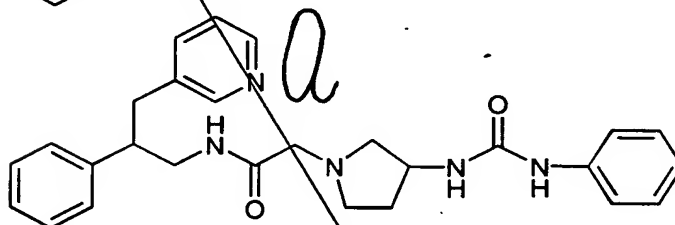
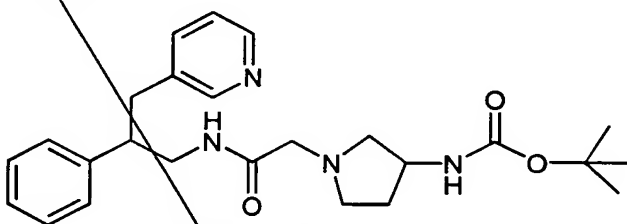
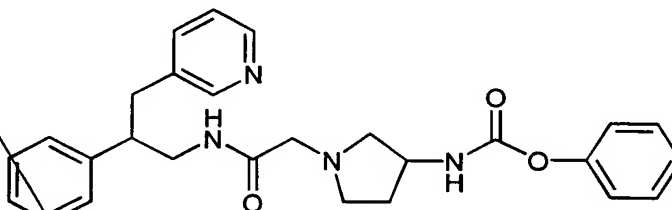
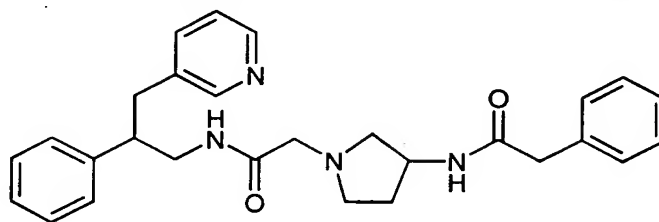
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and

and

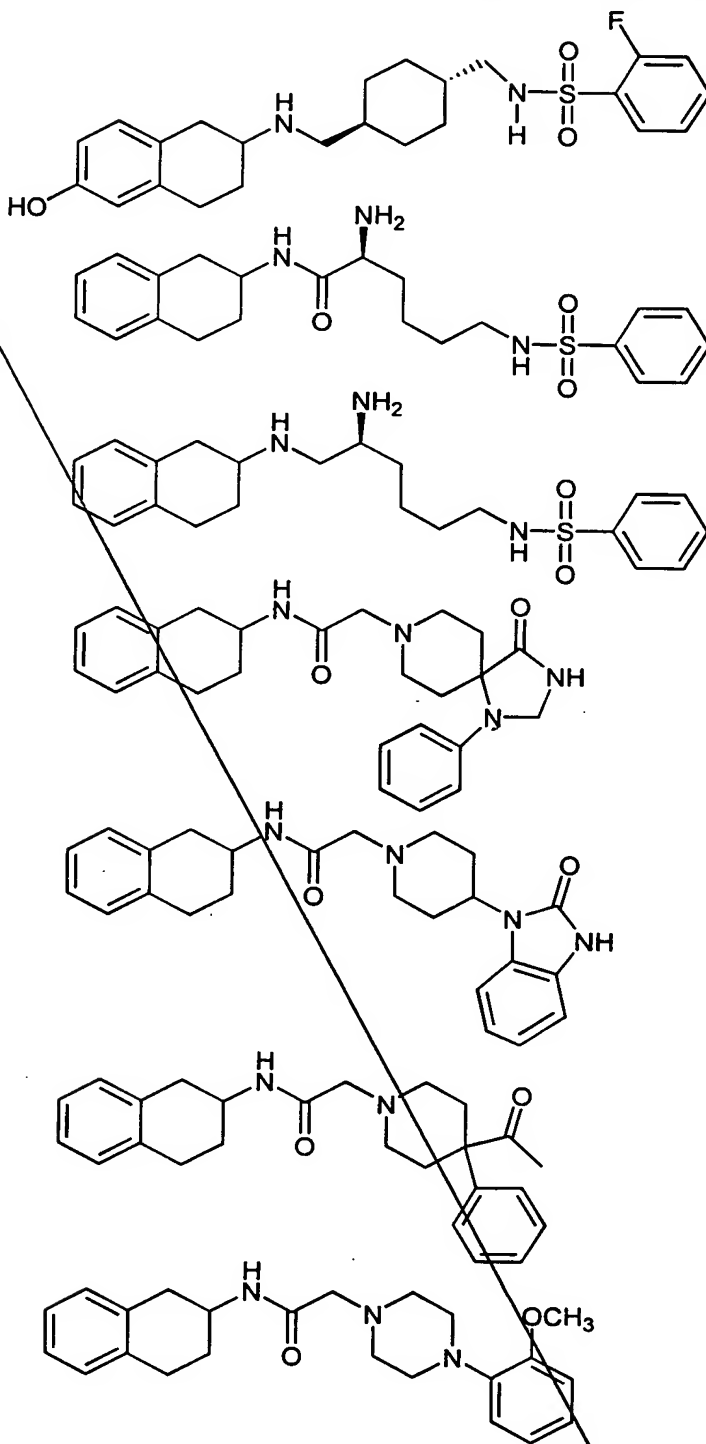
11. A compound of claim 1 selected from the group consisting of:



and

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12. A compound of claim 1 selected from the group consisting of:



and

13. A compound of claim 1 selected from the group consisting of:

2-Amino-6-[(2-fluorophenylsulfonyl)amino]-N-[*cis*-1,2,3,4-tetrahydro-6-methoxy-1-(3-pyridinylmethyl)-2-naphthenyl-(2S)-hexanamide bis-hydrochloride,

N-[5-amino-6-[[*cis*-1,2,3,4-tetrahydro-6-methoxy-1-(3-pyridinylmethyl)-2-naphthalenyl]amino]hexyl-2-fluorobenzenesulfonamide tris-hydrochloride,

N-[5-amino-6-[[*cis*-1,2,3,4-tetrahydro-6-hydroxy-1-(3-pyridinylmethyl)-2-naphthalenyl]amino]hexyl-2-fluorobenzenesulfonamide tris-hydrochloride,

(2S)-2-(Acetylamino)-6-[(2-fluorophenylsulfonyl)amino]-N-[*cis*-1,2,3,4-tetrahydro-6-methoxy-1-(3-pyridinylmethyl)-2-naphthenyl]hexanamide bis-hydrochloride,

(2S)-2-(Acetylamino)-6-[(2-fluorophenylsulfonyl)amino]-N-[*cis*-1,2,3,4-tetrahydro-6-hydroxy-1-(3-pyridinylmethyl)-2-naphthenyl]hexanamide bis-hydrochloride,

3-[(Phenylsulfonyl)amino]-N-[*cis*-1,2,3,4-tetrahydro-6-fluoro-1-(3-pyridinylmethyl)-2-naphthalenyl]-1-pyrrolidineacetamide bis-trifluoroacetate,

4-(2,3-Dihydro-2-oxo-1*H*-benzimidazol-1-yl)-N-[*cis*-1,2,3,4-tetrahydro-6-methoxy-1-(3-pyridinylmethyl)-2-naphthalenyl]-1-piperidineacetamide bis-hydrochloride,

4-(2,3-Dihydro-2-oxo-1*H*-benzimidazol-1-yl)-N-[*trans*-1,2,3,4-tetrahydro-6-methoxy-1-(3-pyridinylmethyl)-2-naphthalenyl]-1-piperidineacetamide bis-hydrochloride,

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4-Acetyl-4-phenyl-N-[*cis*-1,2,3,4-tetrahydro-1-(3-pyridinylmethyl)-2-naphthalenyl]-1-piperidineacetamide bis-hydrochloride,

5 4-Oxo-1-phenyl-N-[*cis*-1,2,3,4-tetrahydro-1-(3-pyridinylmethyl)-2-naphthalenyl]-1,3,8-triazaspiro[4.5]decane-8-acetamide bis-hydrochloride,

10 4-(2,3-Dihydro-2-oxo-1*H*-benzimidazol-1-yl)-N-[*cis*-1,2,3,4-tetrahydro-6-hydroxy-1-(3-pyridinylmethyl)-2-naphthalenyl]-1-piperidineacetamide bis-hydrochloride,

15 *trans*-N-[2-(4-fluorophenyl)-3-(3-pyridinyl)propyl]-4-(((2-fluorophenylsulfonyl)amino)methyl)-1-cyclohexanamide hydrochloride,

trans-N-[[[2-(4-fluorophenyl)-3-(3-pyridinyl)propyl]amino]methyl]-4-cyclohexyl]methyl] 2-fluorobenzenesulfonamide bis-hydrochloride and

20 N-[2-(4-fluorophenyl)-3-(3-pyridinyl)propyl]-4-[(2-fluorophenylsulfonyl)amino]-1-piperidineacetamide bis-trifluoroacetate.

14. A method of treating disorders and diseases associated with NPY receptor subtype 5 comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of claim 1.

15. A pharmaceutical composition for the treatment of diseases or disorders associated with the NPY Y5 receptor subtype comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

16. A pharmaceutical composition according to claim 15 for the treatment of disorders or disease states caused by eating disorders, obesity, bulimia

~~nervosa, diabetes, memory loss, epileptic seizures, migraine, sleep disturbances, pain, sexual/reproductive disorders, depression and anxiety.~~

add
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2020-03-14